SYNOPSIS FOR REGISTRATION OF Ph.D

On

Formulation and Evaluation of Nanogel using Biogenic Method for Wound Healing Properties

Submitted

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Submitted By

Miss. Jadhav Shital Shyamsundar

(M. Pharmacy, Pharmaceutics)

Under the guidance of

Dr. R S. Moon

Asst. Professor,

School of Pharmacy

S.R.T.M.University,

Nanded- 431606.

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ABSTRACT OF PRAPOSED WORK PLAN

Herbal therapy and herbal drug predominates in traditional medicine practiced in developed world plant derived substances and herbal medicines have recently attracted the great interest towards their versatile application. The main objective the present study is to formulate and evaluate herbal ointment with antimicrobial activity by using Azadirachta Indica and Bombax Ceiba polymer. The Nanotechnology, a relatively new technology, offers a smart drug delivery and drug manufacturing strategy that involves the design, manufacturing, and characterization of materials or molecules and devices that have appropriate abilities at the nanoscale. Nanogels are three-dimensional hydrogel materials in the nanoscale size range made of cross linked swellable polymer networks with a high capacity to store water without dissolving into the aqueous media. A wide range of naturally occurring polymers, synthesized polymers, or a combination of both can be found in Nanogels. The chemical makeup of the Nanogels can be changed to fine-tune properties like size, charge, porosity, amphiphilicity, softness, and degradability. Most of them are spherical, although modern advances in synthetic techniques enable the manufacturing of Nanogels with various shapes. Traditional therapies generally involve costly and long- lasting treatments, with a wound relapse rate above 70%. Research in the areas of wound healing and skin regeneration is heavily influenced by the increasing numbers of patients starving for better healing outcomes and the enormous budget spent on wound care, which is still rising. Wound healing is a complex mechanism that can be categorized as an allergic response, propagation, and remodeling in three parallel phases. This study will help develop better Nanogels with characteristics and enhance the usefulness of Nanogels for various biomedical application.

INTRODUCTION

Wound is defined as the damage to the integrity of biological tissue, including skin mucous membranes and organ tissues. Various types of traumas can cause these, and it is critical to ensure wounds are cleaned and appropriately dressed to limit the spread of infection and further injury. The wound-healing process involves healing a wound that has been inflicted on the skin and other soft tissues. Inflammation occurs as a result of the injury, and the connective tissues cells under the dermis produce more collagen as a result. The epithelial tissue afterwards regenerates its outer layer. Wound healing is mainly classified into two categories, Primary wound healing, and Secondary wound healing. Primary wound healing is the uncomplicated healing process of non-infected, well-adapted wounds. If the healing process is disturbed by local factors such as infections, dehiscence, inadequate blood perfusion or systemic factors such as immunocompromise, a situation of secondary wound healing develops. The overriding principle of wound management in secondary wound healing is to ensure the presence of a moist, physiological environment. Air and especially oxygen are cytotoxic and, if the wound is allowed to become dry, inevitably lead to extensive tissue necroses which cause irreparable damage especially in capillary-free (bradytrophic) tissue. Wound healing is a complex mechanism that can be categorized as an allergic response, propagation, and remodeling in three parallel phases. The inflammatory process initiates a proliferative wound repair response further characterized by vascular responses like blood coagulation and haemostasis. Cellular activities include leukocyte infiltration with the release of antimicrobials and cytokines. During the proliferative process, the epithelium is formed to coat the wound surface with the subsequent growth of granulation tissue to fill the wound space. The generation of granulation tissue includes fibroblast proliferation, collagen deposition as well as other extracellular matrices, and the development of new blood vessels.

The remodeling process begins to restore structural integrity and functional competence to the tissue when the new tissue is established inside the wound**.** Nanocarriers have been used for a variety of disease therapies as an ideal multifunctional drug delivery system (DDS), including passive targeting because of the enhanced permeability and retention (EPR) effect, active targeting made possible by ligand modification of nanoplatform surfaces, and site-specific and time-controlled drug delivery strategies mediated by stimuli- responsive materials. Different synthetic techniques have been used for developing Nanoparticle with various morphologies and sizes. Although these techniques have produced superior Nanoparticle, a fundamental understanding of improved manufacturing processes is still needed. This knowledge could be applied at the industrial and commercial level to produce products that are more robust, long-

lasting, clean, safe, and intelligent, such as home appliances, communication technology, medicines, transportation, agriculture, and industries. As a result, designing NPs with the environment consideration is the major goal. These offer remedies to the increasing environmental challenges. Different metallic Nanopartcals have been synthesized using a biological method, which offers advantages over other chemical processes since it is less destructive to the environment, energy efficient, and economical. Compared to NPs made by chemical processes, those coated with biological molecules on their surface are more biocompatible[4]. Applications in biomedicine and related sectors are made possible by the biocompatibility of bio-inspired nanoparticle and Secondary wound healing. Primary wound healing is the uncomplicated healing process of non-infected, well-adapted wounds. If the healing process is disturbed by local factors such as infections, dehiscence, inadequate blood perfusion or systemic factors such as immunocompromise, a situation of secondary wound healing develops.

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SELECTION OF HERBAL PLANTS

Various medicinal plants have been used for years in daily life to treat disease all the world. Herbal medicine is making dramatic comeback and increasing number of patients are visiting alternative medicine clinics. Side effects of synthetic medicine are alarming and recent time has seen risk of herbal and herbal-synthetic drug interaction. Traditional medicines if used judiciously can save a lot of time spent in the treatment and thus reducing global burden. Uses of plants and traditional practices will continue to play a significant role in the socio-cultural life of village communities. The herbal drugs and Excipients have more precise action and have no side effects and are economic. Herbal medicine refers to the use of any plants seeds, berries, roots, leaves, bark or flowers for medicinal purposes. Herbal medicine, also called botanical medicine or phyto-medicine, refers to the use of any plant's seeds, berries, roots, leaves, bark or flowers for medicinal purposes. Plants had been used for medicinal purposes long before recorded history, among the various indications where traditional herbal medicines are used as wound healing and skin related disorder. Certain plant exhibits properties like antimicrobial (ex aloevera, calendula officinalis), antinflamatory (Ex. Turmeric), antioxidant (green tea) and tissue

regenerative activities which aid in the different stages of wound healing. These stages include haemostasis, inflammation, proliferation and remodelling.

REVIEW OF LITERATURE

1. **Himaja N.et al (2017):** Formulated and evaluate on herbal cream from *AzardiractaIndica*. The Ethanolic extract of *AzardiractaIndica* exhibited strong Antibacterial activity. Herbal cream which is non toxic, safe, effective and improves patient compliance by the utilization of herbal extract would be highly acceptable. The herbal formulation showed good consistency, Spreadability, homogeneity, P^H, Non greasy and no evidence of phase separation. The herbal extract containing cream substantially increased skin elasticity, hydration and decreased the skin melanin.
2. **Dr. Uma A.P et al (2017):** Studied on Antimicrobial Activity in pulp extracts of Neem*AzadirachtaIndica* .In this study it was assess the antimicrobial activity of *Azadirachta Indica* against pulp extract human pathogenic bacteria pathogen. *Azadirachta Indica* pulp extract showed strong antimicrobial Activity against selected bacterial species studied at all the concentration tested and had exhibited potent antibacterial activity against various strains of bacterial pathogens. Phytochemical analysis of the aqueous extract of the pulp reveled. The presence of alkaloids, reducing sugar, saponins etc. so the pulp extract of Neem are good for human consumption.
3. **Kamble et al (2017):** Studied on phamarcognostic and pharmacological studies of *Bombaxceiba thorn* extract. The study revealed the physicochemical and phamarcognostic features of thorn of *Bombaxceiba* and highlighted key features. The presence of wide range of physicochemical was preliminary determined. The study also revealed the possession of various potential like anti-inflammatory, antioxidant, anthelmintic and antimicrobial activity against nosocomial infection opens new future prospective of these thorns which is early literature were considered hard structure.
4. **Shubhangi E.Sawant.et al (2016):** Had studied on formulated herbal ointment containing Neem *(Azadirachta Indica)* and *Turmeric (curcuma Longa)* extract. The Ethanolic extracts were prepared by maceration method. The ointment base was done by incorporation the extract in the base by levigation method. After completion of formulation it was evaluated for physicochemical parameter and also formulation was evaluated for its stability at various temperature conditions which shows no change in the irritancy, Spreadability and diffusion study. Neem acts as a antiseptic, insecticide,

Antifertility and Antiviral it could become a media to use the medicinal probe of Neem and turmeric effectively and easily simple dosage form.

5. **Donipati el al(2015):**

   Had studied on Antimicrobial Activity of flower extract of *Bombaxceiba* on coli forms. The aim of the study to assess the antimicrobial activity and to determine zone of inhibition of extracts on some bacterial strains. In the present study, the microbial activity of hexane, Methanol and chloroform, extract of flowers of *Bombaxceiba*were evaluated form potential antimicrobial activity against medically important bacterial strains. The antimicrobial activity was determined in the extract using agar disc diffusion method. The extract showed broad spectrum of inhibition by showing antibacterial effect for both gram positive and gram negative bacterial strains. Among all organisms studied result concluded that *Bombaxceiba* showed best antimicrobial property.

6. **Yallapu MM, et al. (2011)**

   This study provides a comprehensive insight into current advances in the use of Nanogels-mediated chemotherapy for cancer treatment. Nanogels are composed of cross-linked three-dimensional polymer chain networks that are formed via covalent linkages or self-assembly processes. The porosity between the cross-linked networks of Nanogels not only provides an ideal reservoir for loading drugs, oligonucleotides and imaging agents, but also protects them from environmental degradation and hazards. In this study, they mainly focus the novel synthetic strategies and key considerations in the design of Nanogels-based drug delivery systems for controlled and targeted cancer therapeutic applications.

7. **Yashashri I, et al. (2018)**

   This study proposed to formulate nanosizes dispersion of Beta sitosterol by nanoprecipitation method and incorporating it into the gelling agent to produce Nanogels by dispersion method. 1% of carbopol 934 shows better in-vitro drug release than the other concentrations of carbopol 934.

8. **Talele S, et al. (2017)**

   This study proposed to formulate and evaluate Nanogels containing diclofenac sodium for the transdermal/topical preparation. The Nanogels was formulated and optimized for homogeneity, particle size, pH, drug content, in vitro drug release, skin irritation test, spread ability, extrudability, and viscosity. The formulated Nanogels were administered through the dermal route and the initial release rate from each formulation was very rapid, this may be due to incomplete gel formation in the earlier time period, but the

release became slow in latter period after complete gel formation. The release profiles exhibited an inflection point, which indicated gel formation on the diffusion membrane in donor compartment of diffusion cell. During gel formation, formulation got converted into the gel phase and thus drug release became slow. The results showed that the formed gels had the ability to retain diclofenac sodium for the duration.

9. **Phatak AA, et al. (2012)**

   This study proposed to formulate novel Nanogels form which represents an effective and better carrier for the transdermal/topical preparations. The prepared Nanogels formulation showed the better penetration in the skin may be due to the enhanced contact between the drug and the skin resulting from more surface area and hydration. The formulation showed stability over the study period and showed substantial increase in the efficacy in animal studies. The prepared formulation proves to be the better alternative for the oral administration of aceclofenac (NSAID) and eliminates the limitations of the drug like gastric disturbances, low bioavailability; short half live and first pass effect.

10. **Goncalves C, et al. (2012)**

    This study proposed that the self-assembled Nanogels obtained from hydrophobically modified dextrin are effective curcumin Nanocarriers. The stability and loading efficiency of curcumin-loaded Nanogels depends on the Nanogels/curcumin ratio. Higher stability of the formulation is achieved in water than in PBS buffer, as evaluated by dynamic light scattering and fluorescence measurements. The in vitro release profile, using sink conditions, indicates that dextrin Nanogels may perform as a suitable carrier for the controlled release of curcumin. Biological activity of curcumin-loaded Nanogels in HeLa cell cultures was assessed using the MTS assay.

11. **Yu S, et al. (2006)**

    This proposed study reports the manufacture of stable, narrowly distributed Nanogels (hydrodynamic radius about 100 nm) using a novel and convenient method: ovalbumin and lysozyme solutions were mixed at pH 5.3, the mixture solution was adjusted to pH 10.3, then subsequently stirred and heated. The Nanogels were characterized using a combination of techniques. The Nanogels have spherical shape and core-shell structure. The core is mainly composed of lysozyme and the shell is mainly composed of ovalbumin. The proteins in the Nanogels are in denatured states and they are bound by intermolecular hydrophobic interactions, hydrogen bonds, and disulfide bonds. The charges of the Nanogels can be modulated by the pH of the medium. The electrostatic

repulsion of ovalbumin molecules on the Nanogels surface stabilizes the Nanogels in aqueous solution.

12. Dev SK, et al. (2018)

This study proposed to evaluate the antimicrobial, anti-inflammatory and wound healing activity of polyherbal formulation. The findings of the study revealed the synergistic antimicrobial potential of Polyherbal drug against gram-positive and negative strains. Polyherbal carbopol- 940 gels (2% and 5%w/w) promoted the wound healing and anti-inflammatory effect. The high rate of wound contraction (< 0.0001), early epithelialization period (< 0.0001) and increased wound breaking strength (< 0.0001) were observed in 2% and 5% polyherbal gel treated group when compared to the normal control and negative control group. Also, study revealed the antimicrobial and anti-inflammatory effect of Polyherbal drug provoked and promoted the wound healing process through accelerated remodeling of damaged tissue.

OBJECTIVE OF RESEARCH

1. Collection, Extraction, Purification and preliminary evaluation and Identification of Natural Plant.
2. To design, formulate and evaluate herbal Nano gels by using biogenic method.
3. Check Antimicrobial, Antibacterial, Antifungal Activity of Topical Drug Delivery.
4. To improve the efficacy, drug loading capacity and biocompatibility of drugs by formulating in Nano gels.
5. To study stability of optimized formulation.
6. To evaluate wound healing potential of herbal Nano gels by in-vivo or in-vitro study.

METHODOLOGY:

1. Collection of different parts of the plants and authentication of plants.
2. Extraction of plant parts by using various solvents and extraction processes.
3. Phytochemical screening of different extracts and fractions using standard tests.
4. By using the above evaluation data, preparation of different herbal formulations to give Antimicrobial, Antifungal, Antibacterial activity.
5. Evaluation of these herbal formulations by using various Evaluation test.

PROPOSED WORKS PLAN:

First Year:

- Collection of plant material, identification of plants.
- Preparation of extracts by using various solvents, procurement, drying of extracts
- Phytochemical screening of extracts
- Preparation of nanoparticle study
- Evaluation, preliminary studies and main studies.

Second year:

- Fractionation of potent extract
- Antimicrobial, Antifungal, Antibacterial activity of selected fractions
- Separation and isolation of compound by analytical chromatography technique.

Third year:

- Preparation of herbal formulation
- Formulation of herbal Nanogels by using biogenic method
- **Evaluation of Nanogels -**Particle size and zeta potential measurement**,** Surface morphology by scanning gel ectron microscopy, Entrapment efficiency, Physical parameters, FT-IR XRD, Transmission electron microscopy (TEM).
- Stability studies as per ich guidelines.
- Wound healing evaluation of selected formulation.

SIGNIFICANCE OF STUDY:

1. The significance of study wound healing Nanogels produced by biogenic method lies in their potential to wound care through environmentally sustainable and biocompatible innovation.
2. Biocompatibility and safety- biogenic method utilizes natural materials such as plant extract, microbes or biomolecules which reduce the risk of toxicity and ensure compatibility with human tissue this minimize side effect making them safer for the patient compare to synthetic formulation
3. Enhance wound healing-Nanogels provide moist environment and control drug release, accelerating the healing process, they can incorporated bioactive compound (ex. antimicrobial agent, growth factor) that promote tissue regeneration and prevent infection.
4. Biogenic approaches involve green chemistry principle using renewable resources and avoiding harmful chemicals so it is ecofrindly synthesis.
5. Potential for customization-biogenic Nanogels can be tailored to specific wound type (ex, chronicwound,burn). By adjusting their composition and functional additives, this versatility enhance their clinical applicability.
6. Cost Effectiveness-Utilizing natural resources and low energy synthesis method can lower production cost making.
7. Hence wound healing Nanogels develop through biogenic method will represent a sustainable, efficient and patient friendly advancement in medical science.

REFERENCES

1. Sawant S.E, Tajane. M.D. Formulation and Evaluation of herbal ointment containing Neem and Turmeric extract. Journal of scientific and Innovative Reseach.2016; 5(4):149-151.
2. H.P.Rajashree, George J, Sebastain.G ,GowdaD.V.Formulation and Phytochemical screening and physico-chemical evaluation of an antiseptic ointment containing Azadirachta Indica And chromolenaodorata. Internationational journal off Pharmacy and Biological Sciences.2015; 5(4):114-118.
3. Himajaetal.Formulation and Evaluation of Herbal cream from Azadirachta Indica Ethanolic Extract. International Journal of Research in Drug and Pharmaceutical science.2017; 1(1):23-27.
4. Mishra A, Panola R, Vyas B, Marothia D, Kansara H.International Journal of Pharmaceutical Erudition Review Article; Topical antibiotics and Semisolid Dosage Forms.2014; 4(3): 33-54.
5. Dev.A, Chodankar, Shelke.O. Emulgels: a novel topical drug delivery system Review Article: Pharmaceutical and Biological Evaluations. 2015; 2 (4): 64-75.Raut.P.N, Nayak.S.V, Gotmare.S.R. Research Article on Bombaxceiba. International Journal of Advanced Research.2017; 5(2):1211-1214.
6. Vandana.M,chaudhary.A.K.Shalmali(BombaxCeiba):VersatilityTherapeutics.International Journal on Green Pharmacy.2017;11(3):401-406.
7. Donipati.R.Subhasini.P. Determining the antioxidant Activity of Bombaxceiba Flower Extracts. International Journal for Pharmaceutical Research Scholors.2016; 5(1):146-150.
8. Bhargava.S, Shah.M.B. Evaluation of Hypoglycemic activity of different Extracts of Bombaxceiba L.leaves.Research.J.Pharm.and.Tech.2016; 9(3):361-364.
9. Rehaman FAL, Maqbool F, Elmina EI, Shayoub ME, Elhaasan AM, Hussaein SEO. Nanogel a Pharmaceutical Carrier- Review Article. SJAMS. 2017;5(11F):4730-4736.
10. Torchilin V.P. Multifunctional, stimuli-sensitive nanoparticulate systems for drug delivery. Nat. Rev. Drug Discover. 2014; 13:813-827.
11. Soni KS, Desale SS, Bronich TK. Nanogels: An overview of properties, biomedical applications, and obstacles to clinical translation. Journal of Controlled Release. 2016; 240:109-126.

12. Hakim LF, Portman JL, Casper MD, Weimer AW. Aggregation behavior of nanoparticle in fluidized beds. Powder Technology. 2005; 106(3):149-160.
13. Huang J, Lin L, Sun D, Chen S, Yang D, Li Q. Bio-inspired synthesis of metal nonmaterial's and applications. Chem Soc Rev. 2015;44:6330-6374.
14. Kujath P, Michelsen A. Wounds - from physiology to wound dressing. DtschArztebl Int. 2008; 105(13):239-48.
15. Enyedi B, Niethammer P. Mechanisms of epithelial wound detection. Trends Cell Biol. 2015;25(7):398-407.
16. Leoni G, Neumann PA, Sumagin R, Denning TL, Nusrat A. Wound repair: role of immune-epithelial interactions. Mucosal Immunol. 2015;8(5):959-68.
17. Garcia-Orue I, Gainza G, Villullas S, Pedraz JL, et al. Nanotechnology approaches for skin wound regeneration using drug-delivery systems. 2016;31–55.
18. Sharma A, Khanna S, Kaur G, Singh I. Medicinal plants and their components for wound healing applications. Future Journal of Pharmaceutical Sciences. 2021;7(53):113.
19. Yallapu MM, Jaggi M, Chauhan SC. Design and engineering of Nanogels for cancer treatment. DrugDiscovToday.2011; 16(9-10):457-63.
20. Yashashri, Bhushan R, AshishJ. Preparation, and evaluation of betasitosterolnanogel:a carrier design for targeted drug delivery system. Asian Journal of Pharmaceutical Research and Development. 2018;6(3):81-87.
21. Talele S, Nikam P, Ghosh B, Deore C. A Research Article on Nanogel as Topical Promising Drug Delivery for Diclofenac sodium. Indian Journal of Pharmaceutical Education and Research.2017;51(4S):S580-S587.
22. Phatak AA, Chaudhari PD. Development and Evaluation of Nanogel as a Carrier for Transdermal Delivery of Aceclofenac. AsianJ. Pharm.Tech. 2012;2(4):125-132.
23. Gonçalves C, Pereira P, Schellenberg P, Coutinho PJ, et al. Self-Assembled DextrinNanogelasCurcuminDeliverySystem.JournalofBiomaterialsandNanobiotechnology.2012;3(2):178-184.
24. Yu S, Yao P, Jiang M, Zhang G. Nanogels prepared by self-assembly of oppositely charged globular proteins. Biopolymers.2006;83(2):148-58.
25. Dev SK, Chaudhari PK, Srivastava R, Sharma M. Antimicrobial, anti-inflammatoryandwoundhealingactivityofpolyherbalformulation.Biomedicine&Pharmacotherapy.2018;111(2019):555-567.